Biophysical characteristics reveal neural stem cell differentiation potential.

Journal: PLoS One

Publication Year: 2011

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PubMed link: 21980464

Funding Grants: Novel Separation of Stem Cell Subpopulations, UCI-CIRM Research Training Program II

Public Summary:
Distinguishing human neural stem/progenitor cell (huNSPC) populations that will predominantly generate neurons from those that produce glia is currently hampered by a lack of sufficient cell type-specific surface markers predictive of fate potential. This limits investigation of progenitors and their potential use as therapeutic agents. A live-cell biophysical and label-free measure of fate potential would solve this problem by reducing the need for specific cell surface markers. We used dielectrophoresis (DEP) to analyze the biophysical, specifically electrophysiological, properties of cortical human and mouse NSPCs that vary in differentiation potential. Our data demonstrate that the electrophysiological property membrane capacitance inversely correlates with the neurogenic potential of NSPCs. Furthermore, as huNSPCs are continually passaged they decrease neuron generation and increase membrane capacitance, confirming that this parameter dynamically predicts and negatively correlates with neurogenic potential. In contrast, differences in membrane conductance between NSPCs do not consistently correlate with the ability of the cells to generate neurons. DEP crossover frequency, which is a quantitative measure of cell behavior in DEP, directly correlates with neuron generation of NSPCs, indicating a potential mechanism to separate stem cells biased to particular differentiated cell fates. We show here that whole cell membrane capacitance, but not membrane conductance, reflects and predicts the neurogenic potential of human and mouse NSPCs. Stem cell biophysical characteristics therefore provide a completely novel and quantitative measure of stem cell fate potential and a label-free means to identify neuron- or glial-biased progenitors.

Scientific Abstract:
BACKGROUND: Distinguishing human neural stem/progenitor cell (huNSPC) populations that will predominantly generate neurons from those that produce glia is currently hampered by a lack of sufficient cell type-specific surface markers predictive of fate potential. This limits investigation of lineage-biased progenitors and their potential use as therapeutic agents. A live-cell biophysical and label-free measure of fate potential would solve this problem by obviating the need for specific cell surface markers.
METHODOLOGY/PRINCIPAL FINDINGS: We used dielectrophoresis (DEP) to analyze the biophysical, specifically electrophysiological, properties of cortical human and mouse NSPCs that vary in differentiation potential. Our data demonstrate that the electrophysiological property membrane capacitance inversely correlates with the neurogenic potential of NSPCs. Furthermore, as huNSPCs are continually passaged they decrease neuron generation and increase membrane capacitance, confirming that this parameter dynamically predicts and negatively correlates with neurogenic potential. In contrast, differences in membrane conductance between NSPCs do not consistently correlate with the ability of the cells to generate neurons. DEP crossover frequency, which is a quantitative measure of cell behavior in DEP, directly correlates with neuron generation of NSPCs, indicating a potential mechanism to separate stem cells biased to particular differentiated cell fates. CONCLUSIONS/SIGNIFICANCE: We show here that whole cell membrane capacitance, but not membrane conductance, reflects and predicts the neurogenic potential of human and mouse NSPCs. Stem cell biophysical characteristics therefore provide a completely novel and quantitative measure of stem cell fate potential and a label-free means to identify neuron- or glial-biased progenitors.